BONE

Gut immune status affects bone mass in mice

The absence of a gut microbiota increases bone mass in mice, report Klara Sjögren and colleagues in the *Journal of Bone and Mineral Research*.

The gut microbiota affects immune status and can stimulate endocrine cells in the gut to release hormones. Gut-associated inflammatory and autoimmune conditions have been associated with low bone mass, and gut-derived serotonin has been shown to have a negative effect

on bone formation in mice, suggesting a connection between the gut and bone. Sjögren and colleagues set out to investigate the effect of the gut microbiota on bone mass in mice.

The researchers assessed bone mass in 7-week-old female germ-free mice and conventionally raised female mice. Germ-free mice had increased proximal tibial volumetric BMD compared with conventionally raised mice ($277 \pm 14 \text{ mg/cm}^3$ versus $208 \pm 10 \text{ mg/cm}^3$, $P \leq 0.01$) as determined by peripheral quantitative CT. The bone volume:tissue volume ratio was also increased (by 39.4%) in germ-free mice. Of note, colonization of germ-free mice with normal gut microbiota brought bone mass to normal levels.

Germ-free mice have previously been shown to exhibit reduced expression of inflammatory cytokines in the spleen, which suggests that the gut microbiota has a role in shaping systemic immunity. “We extended these data by showing that bone marrow from germ-free mice has a reduced frequency of CD4⁺

T cells,” says Sjögren. In addition, bone histomorphometry revealed a reduced number of bone-resorbing osteoclasts and osteoclast precursor cells in the bone marrow of germ-free mice. Furthermore, germ-free mice had decreased levels of gut-derived serotonin.

Sjögren and colleagues conclude that a decreased frequency of CD4⁺ T cells in bone marrow is associated with a decreased expression of inflammatory cytokines and decreased osteoclastogenesis in the absence of gut microbiota. The results indicate that the gut microbiota is a major regulator of bone mass in mice.

Sjögren hopes that these findings open up novel therapeutic opportunities to prevent bone loss or increase bone mass, for example by giving probiotics to patients with conditions such as osteoporosis.

Lian Evans

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